Mohamed
603713

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=> fil reg
COST IN U.S. DOLLARS                                  SINCE FILE    TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.15       0.15

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DICTIONARY FILE UPDATES:  13 SEP 2001  HIGHEST RN 356757-49-8

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> e memapsin 2/cn 5
E1            1     MEMAPSIN (HUMAN ISOFORM 2 C-TERMINAL FRAGMENT)/CN
E2            1     MEMAPSIN 1/CN
E3            1 --> MEMAPSIN 2/CN
E4            2     MEMAPSIN 2 PEPTIDE SUBSTRATE (SYNTHETIC)/CN
E5            1     MEMBANE PROTEIN, CATION EFFLUX PUMP (MDR-TYPE)
(CLOSTRIDIUM
                    ACETOBUTYLICUM STRAIN ATCC 824 GENE CAC2485)/CN

=> s e3;d ide can
L1            1 "MEMAPSIN 2"/CN


L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   158736-49-3  REGISTRY
CN   .beta.-Secretase (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   .beta. Protein amyloidogenase
CN   .beta.-Amyloid protein precursor secretase
CN   .beta.-Site APP-cleaving enzyme
CN   .beta.-site APP-cleaving enzyme 1
CN   .beta.-site APP-cleaving enzyme 2
CN   Amyloid precursor protein secretase
CN   APP secretase
CN   Aspartic protease BACE
CN   Aspartic protease BACE1
CN   Aspartic protease BACE2
CN   Memapsin 1
CN   Memapsin 2
CN   Protease Asp1
CN   Protease Asp2
MF   Unspecified
CI   MAN
```


Prepared by M. Hale 308-4258

```
SR   CA
LC   STN Files:   BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PROMT, TOXLIT,
       USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             345 REFERENCES IN FILE CA (1967 TO DATE)
               4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             349 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  135:179013

REFERENCE   2:  135:179012

REFERENCE   3:  135:178989

REFERENCE   4:  135:176843

REFERENCE   5:  135:175406

REFERENCE   6:  135:165420

REFERENCE   7:  135:149611

REFERENCE   8:  135:146686

REFERENCE   9:  135:135817

REFERENCE  10:  135:132456


=> e "om-99-1"/cn 5
E1            1     OM-518/CN
E2            1     OM-977/CN
E3            0 --> OM-99-1/CN
E4            1     OM-FURAN/CN
E5            1     OM-TUSSIC/CN

=> e "om99-1"/cn 5
E1            1     OM-TUSSIS/CN
E2            1     OM9/CN
E3            0 --> OM99-1/CN
E4            1     OMACICLOVIR/CN
E5            1     OMACIDE 24/CN

=> e dipeptide isostere/cn 5
E1            1     DIPEPTIDE ARYLAMIDASE I/CN
E2            1     DIPEPTIDE HYDROLASE/CN
E3            0 --> DIPEPTIDE ISOSTERE/CN
E4            1     DIPEPTIDE PERMEASE/CN
E5            1     DIPEPTIDE PERMEASE (ESCHERICHIA COLI STRAIN MM500 GENE
DPPA
                    PRECURSOR)/CN

=> s l.a/sqsp
L2      450062 L.A/SQSP
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=> s l2(l)dipeptide

           147 DIPEPTIDE
L3           0 L2(L)DIPEPTIDE

=> s l2(l)isostere
             0 ISOSTERE
L4           0 L2(L)ISOSTERE

=> fil medl,caplus,biosis,embase,wpids,jicst;s (l1 or memapsin 2) and
(alzheimer? or om99! or om-99! or dipeptide isostere or dipeptide or isostere)
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                     40.14      40.29

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L5           4 FILE MEDLINE
L6         297 FILE CAPLUS
L7         217 FILE BIOSIS
L8           6 FILE EMBASE
L9           2 FILE WPIDS
L10          0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L11        526 (L1 OR MEMAPSIN 2) AND (ALZHEIMER? OR OM99! OR OM-99! OR
DIPEPTI
               DE ISOSTERE OR DIPEPTIDE OR ISOSTERE)

=> s (l1 or memapsin 2) and (om99! or om-99! or dipeptide isostere or
dipeptide or isostere) and alzheimer?
L12          1 FILE MEDLINE
L13          5 FILE CAPLUS
L14          1 FILE BIOSIS
L15          1 FILE EMBASE
L16          2 FILE WPIDS
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Prepared by M. Hale 308-4258

L17 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L18 10 (L1 OR MEMAPSIN 2) AND (OM99! OR OM-99! OR DIPEPTIDE ISOSTERE OR DIPEPTIDE OR ISOSTERE) AND ALZHEIMER?

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PROCESSING COMPLETED FOR L18
L19 6 DUP REM L18 (4 DUPLICATES REMOVED)

=> d cbib abs 1-6

priority claimed

L19 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2001:12489 Document No. 134:80832 Inhibitors of **memapsin 2** and use thereof. Tang, Jordan J. N.; Hong, Ling; Ghosh, Arun K. (Oklahoma Medical Research Foundation, USA; The Board of Trustees of the University of Illinois). PCT Int. Appl. WO 2001000665 A2 20010104, 86 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US17742 20000627. PRIORITY: US 1999-PV141363 19990628; US 1999-PV168060 19991130; US 2000-PV177836 20000125; US 2000-PV178368 20000127; US 2000-PV210292 20000608.

AB Methods for the prodn. of purified, catalytically active, recombinant **memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been detd. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can inhibit the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including **isosteres** at the sites of the crit. amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Figure 1). The inhibition const. of OM99-2 is 1.6 x 10-9 M against recombinant pro-**memapsin 2**. Crystallog. of **memapsin 2** bound to this inhibitor was used to det. the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new inhibitors, using com. available software programs and techniques familiar to those in org. chem. and enzymol., to design new inhibitors to **memapsin 2**, useful in diagnostics and for the treatment and/or prevention of

Alzheimer's disease.

L19 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
2001:12487 Document No. 134:68049 Catalytically active recombinant **memapsin 2**, 3D crystal structure based inhibitor design, synthesis, and screening, for **Alzheimer**'s disease treatment. Tang, Jordan J. N.; Lin, Xinli; Koelsch, Gerald (Oklahoma Medical Research Foundation, USA). PCT Int. Appl. WO 2001000663 A2 20010104, 87 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US17661 20000627. PRIORITY: US 1999-PV141363 19990628; US 1999-PV168060 19991130; US 2000-PV177836 20000125; US 2000-PV178368 20000127; US 2000-PV210292 20000608.

AB A method for producing catalytically active recombinant **memapsin 2** comprising expression in a bacteria and refolding the recombinant **memapsin 2** under conditions which dissoc. and then slowly refold the enzyme into a catalytically active form is disclosed. A method of isolating inhibitors of cleavage by **memapsin 2** comprising adding to one or more potential inhibitors of catalytically active recombinant **memapsin 2**, and a substrate for **memapsin 2**, and screening for decreased cleavage of the substrate by the inhibitors, wherein the inhibitors are in a library of small synthetic mols., like proteins and peptides. Alternatively, the inhibitors are oligonucleotides preventing or decreasing expression of catalytically active **memapsin 2**. A method for designing or obtaining inhibitors of catalytically active **memapsin 2** comprising modeling an inhibitor based on the crystn. coordinates of **memapsin 2** or parameters. A database comprising binding properties and chem. structures of compds. designed or screened by modeling an inhibitor based on the crystn. coordinates of **memapsin 2** or parameters is claimed. A method of treating or preventing **Alzheimer**'s disease comprising administering to a patient in need thereof an inhibitor of **memapsin 2** which binds to the active site of the **memapsin 2** defined by the presence of two catalytic aspartic residues and substrate binding cleft, is also claimed. The cDNAs of two new human membrane-assocd. aspartic proteases, memapsin 1 and **memapsin 2**, have been cloned and sequenced. The substrate and subsite specificity of the catalytically active enzyme have been detd. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can inhibit the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by

memapsin 2. Processes for the synthesis of two substrate analogs including **isosteres** at the sites of the crit. amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Fig. 1). The inhibition const. of OM99-2 is 1.6 x 109 M against recombinant pro-**memapsin 2**. Crystallog. of **memapsin 2** bound to this inhibitor was used to det. the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used to design new inhibitors, using com. available software programs and techniques familiar to those in org. chem. and enzymol., to design new inhibitors to **memapsin 2**, useful in diagnostics and for the treatment and/or prevention of **Alzheimer**'s disease.

L19 ANSWER 3 OF 6 MEDLINE DUPLICATE 3
2001489257 Document Number: 21404970. PubMed ID: 11513577. Subsite specificity of **memapsin 2** (beta-secretase): implications for inhibitor design. Turner R T 3rd; Koelsch G; Hong L; Castenheira P; Ghosh A; Tang J. (Protein Studies Program, Oklahoma Medical Research Foundation, and Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73104, USA.) BIOCHEMISTRY, (2001 Aug 28) 40 (34) 10001-6. Journal code: A0G; 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

Not printed out

AB **Memapsin 2** is the protease known as beta-secretase whose action on beta-amyloid precursor protein leads to the production of the beta-amyloid (Abeta) peptide. Since the accumulation of Abeta in the brain is a key event in the pathogenesis of **Alzheimer**'s disease, **memapsin 2** is an important target for the design of inhibitory drugs. Here we describe the residue preference for the subsites of **memapsin 2**. The relative k(cat)/K(M) values of residues in each of the eight subsites were determined by the relative initial cleavage rates of substrate mixtures as quantified by MALDI-TOF mass spectrometry. We found that each subsite can accommodate multiple residues. The S(1) subsite is the most stringent, preferring residues in the order of Leu > Phe > Met > Tyr. The preferences of other subsites are the following: S(2), Asp > Asn > Met; S(3), Ile > Val > Leu; S(4), Glu > Gln > Asp; S(1)', Met > Glu > Gln > Ala; S(2)', Val > Ile > Ala; S(3)', Leu > Trp > Ala; S(4)', Asp > Glu > Trp. In general, S subsites are more specific than the S' subsites. A peptide comprising the eight most favored residues (Glu-Ile-Asp-Leu-Met-Val-Leu-Asp) was found to be hydrolyzed with the highest k(cat)/K(M) value so far observed for **memapsin 2**. Residue preferences at four subsites were also studied by binding of **memapsin 2** to a combinatorial inhibitor library. From 10 tight binding inhibitors, the consensus preferences were as follows: S(2), Asp and Glu; S(3), Leu and Ile; S(2)', Val; and S(3)', Glu and Gln. An inhibitor, OM00-3, Glu-Leu-Asp-LeuAla-Val-Glu-Phe (where the asterisk represents the hydroxyethylene tansition-state

isostere), designed from the consensus residues, was found to be the most potent inhibitor of **memapsin 2** so far reported (K(i) of 3.1 x 10(-10) M). A molecular model of OM00-3 binding to **memapsin 2** revealed critical improvement of the interactions between inhibitor side chains with enzyme over a previous inhibitor, OM99-2 [Ghosh, A. K., et al. (2000) J. Am. Chem. Soc. 14, 3522-3523].

L19 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
2000:455820 Document No. 133:234317 L-685,458, an Aspartyl Protease Transition State Mimic, Is a Potent Inhibitor of Amyloid .beta.-Protein Precursor .gamma.-Secretase Activity. Shearman, Mark S.; Beher, Dirk; Clarke, Earl E.; Lewis, Huw D.; Harrison, Tim; Hunt, Peter; Nadin, Alan; Smith, Adrian L.; Stevenson, Graeme; Castro, Jose L. (Departments of Molecular Biology and Medicinal Chemistry, Merck Sharp & Dohme Research Laboratories The Neuroscience Research Centre, Harlow, CM20 2QR, UK). Biochemistry, 39(30), 8698-8704 (English) 2000. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB Progressive cerebral amyloid .beta.-protein (A.beta.) deposition is believed to play a central role in the pathogenesis of **Alzheimer**'s disease (AD). Elevated levels of A.beta.(42) peptide formation have been linked to early-onset familial AD-causing gene mutations in the amyloid .beta.-protein precursor (A.beta.PP) and the presenilins. Sequential cleavage of A.beta.PP by the .beta.- and .gamma.-secretases generates the N- and C-termini of the A.beta. peptide, making both the .beta.- and .gamma.-secretase enzymes potential therapeutic targets for AD. The identity of the A.beta.PP .gamma.-secretase and the mechanism by which the C-termini of A.beta. are formed remain uncertain, although it has been suggested that the presenilins themselves are novel intramembrane-cleaving .gamma.-secretases of the aspartyl protease class. In this study we report the identification of L-685,458 as a structurally novel inhibitor of A.beta.PP .gamma.-secretase activity, with a similar potency for inhibition of A.beta.(42) and A.beta.(40) peptides. This compd. contains an hydroxyethylene **dipeptide isostere** which suggests that it could function as a transition state analog mimic of an aspartyl protease. The preferred stereochem. of the hydroxyethylene **dipeptide isostere** was found to be the opposite to that required for inhibition of the HIV-1 aspartyl protease, a factor which may contribute to the obsd. specificity of this compd. Specific and potent inhibitors of A.beta.PP .gamma.-secretase activity such as L-685,458 will enable important advances toward the identification and elucidation of the mechanism of action of this enigmatic protease.

L19 ANSWER 5 OF 6 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2000249609 EMBASE Untangling **Alzheimer**'s disease with .beta.-secretase inhibitors. Dorrell S.. Drug Discovery Today 5/8 (316-317) 1 Aug 2000.
Refs: 3.
ISSN: 1359-6446. CODEN: DDTOFS.
Publisher Ident.: S 1359-6446(00)01531-2. Pub. Country: United Kingdom.
Language: English.

L19 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2001 ACS
2000:724245 Document No. 134:53089 Structure of the protease domain of **memapsin 2** (.beta.-secretase) complexed with inhibitor.
Hong, Lin; Koelsch, Gerald; Lin, Xinli; Wu, Shili; Terzyan, Simon; Ghosh, Arun K.; Zhang, Xuenjun C.; Tang, Jordan (Protein Studies Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA). Science (Washington, D. C.), 290(5489), 150-153 (English) 2000. CODEN: SCIEAS. ISSN: 0036-8075. Publisher: American Association for the Advancement of Science.
AB **Memapsin 2** (.beta.-secretase) is a membrane-assocd. aspartic protease involved in the prodn. of .beta.-amyloid peptide in **Alzheimer**'s disease and is a major target for drug design. We detd. the crystal structure of the protease domain of human **memapsin 2** complexed to an eight-residue inhibitor at 1.9 angstrom resoln. The active site of **memapsin 2** is more open and less hydrophobic than that of other human aspartic proteases. The subsite locations from S4 to S2' are well defined. A kink of the inhibitor chain at P2' and the change of chain direction of P3' and P4' may be mimicked to provide inhibitor selectivity.

=> s tang j?/au,in;s hong l?/au,in;s ghosh a?/au,in
'IN' IS NOT A VALID FIELD CODE
L20 905 FILE MEDLINE
L21 2946 FILE CAPLUS
L22 1317 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L23 743 FILE EMBASE
L24 357 FILE WPIDS
L25 193 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L26 6461 TANG J?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L27 130 FILE MEDLINE
L28 468 FILE CAPLUS
L29 266 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L30 157 FILE EMBASE
L31 64 FILE WPIDS
L32 35 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L33 1120 HONG L?/AU,IN

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L34 844 FILE MEDLINE
L35 2533 FILE CAPLUS
L36 1349 FILE BIOSIS

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L39          59 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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u
SEARCH ENDED BY USER

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L46           1 FILE BIOSIS
L47           1 FILE EMBASE
L48           1 FILE WPIDS
L49           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L50          11 L40 AND L33 AND L26

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L51           2 FILE MEDLINE
L52           2 FILE CAPLUS
L53           1 FILE BIOSIS
L54           1 FILE EMBASE
L55           0 FILE WPIDS
L56           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L57           6 L50 NOT L18

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PROCESSING COMPLETED FOR L57
L58           3 DUP REM L57 (3 DUPLICATES REMOVED)

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L58  ANSWER 1 OF 3     MEDLINE                              DUPLICATE 1
2001499125  Document Number: 21412075.     PubMed ID: 11520194.
     Structure-based design: potent inhibitors of human brain memapsin 2
     (beta-secretase). Ghosh A K; Bilcer G; Harwood C; Kawahama R;
     Shin D; Hussain K A; Hong L; Loy J A; Nguyen C; Koelsch G;
     Ermolieff J; Tang J. (Department of Chemistry, University of
     Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607,
     USA.. arunghos@uic.edu) .. JOURNAL OF MEDICINAL CHEMISTRY, (2001 Aug 30)
44
     (18) 2865-8.  Journal code: J0F; 9716531. ISSN: 0022-2623. Pub. country:
     United States. Language: English.
AB   Memapsin 2 (beta-secretase) is one of two proteases that cleave the
     beta-amyloid precursor protein (APP) to produce the 40-42 residue
```

amyloid-beta peptide (Abeta) in the human brain, a key event in the progression of Alzheimer's disease. On the basis of the X-ray crystal structure of our lead inhibitor (2, OM99-2 with eight residues) bound to memapsin, we have reduced the molecular weight and designed potent memapsin inhibitors. Structure-based design and preliminary structure-activity studies have been presented.

L58 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
2001013039 Document Number: 20476770. PubMed ID: 11021803. Structure of the protease domain of memapsin 2 (beta-secretase) complexed with inhibitor. **Hong L**; Koelsch G; Lin X; Wu S; Terzyan S; **Ghosh A K**; Zhang X C; **Tang J**. (Protein Studies Program and Crystallography Program, Oklahoma Medical Research Foundation, 825 NE 13th Street, Oklahoma City, OK 73104, USA.) SCIENCE, (2000 Oct 6) 290 (5489) 150-3. Journal code: UJ7. ISSN: 0036-8075. Pub. country: United States. Language: English.
AB Memapsin 2 (beta-secretase) is a membrane-associated aspartic protease involved in the production of beta-amyloid peptide in Alzheimer's disease and is a major target for drug design. We determined the crystal structure of the protease domain of human memapsin 2 complexed to an eight-residue inhibitor at 1.9 angstrom resolution. The active site of memapsin 2 is more open and less hydrophobic than that of other human aspartic proteases. The subsite locations from S4 to S2' are well defined. A kink of the inhibitor chain at P2' and the change of chain direction of P3' and P4' may be mimicked to provide inhibitor selectivity.

L58 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
2001:667058 Subsite Specificity of Memapsin 2 (.beta.-Secretase): Implications for Inhibitor Design [Erratum for Volume 40, Number 34, August 28, 2001, pages 10001-10006.]. Turner, Robert T., III; Koelsch, Gerald; **Hong, Lin**; Castanheira, Pedro; Ermolieff, Jacques; **Ghosh, Arun K.** ; **Tang, Jordan** Biochemistry ACS ASAP (English). CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
AB Unavailable

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	60.34	100.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.35	-2.35

FILE 'REGISTRY' ENTERED AT 11:57:07 ON 14 SEP 2001
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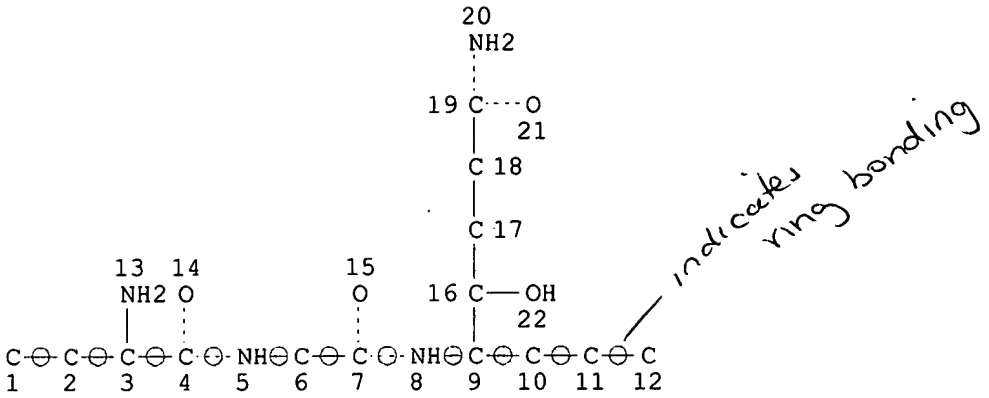
STRUCTURE FILE UPDATES: 13 SEP 2001 HIGHEST RN 356757-49-8



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NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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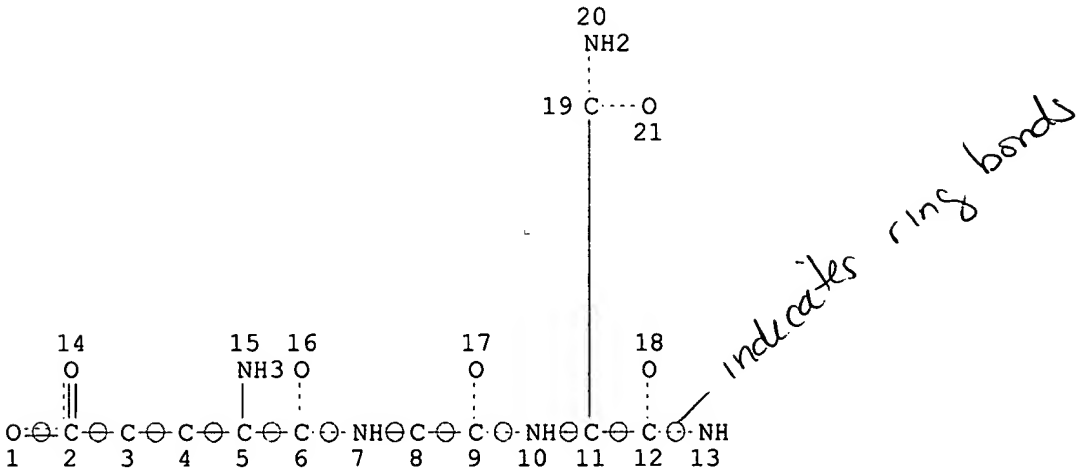
L62 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
L64 0 SEA FILE=REGISTRY SSS FUL L62

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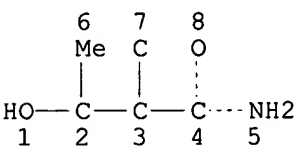
L65 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

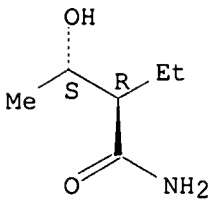
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
L67 28 SEA FILE=REGISTRY SSS FUL L65

100.0% PROCESSED 352658 ITERATIONS 28 ANSWERS
SEARCH TIME: 00.00.09

L67 ANSWER 1 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 216877-20-2 REGISTRY
CN Butanamide, 2-ethyl-3-hydroxy-, (2R,3S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (2R,3S)-2-Ethyl-3-hydroxybutyramide
FS STEREOSEARCH
MF C6 H13 N O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



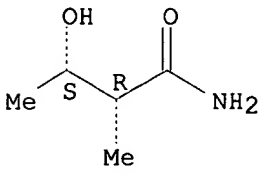
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:51408 Methods and precursors for the production of chiral vicinal amino alcohols. Rozzell, J. David, Jr. (Biocatalytics, Inc., USA). PCT Int. Appl. WO 9854350 A1 19981203, 72 pp. DESIGNATED STATES: RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US10792 19980527. PRIORITY: US 1997-863900 19970527; US 1997-929474 19970915.

AB The disclosure describes a method for the prepn. of chiral vicinal aminoalcs. in high optical purity. The method combines the stereoselective redn. of the keto group of a .beta.-keto acid, .beta.-keto ester, or deriv. with the stereospecific rearrangement of the corresponding amide, hydroxamic acid, or hydrazide to produce chiral vicinal amino alcs. with control of stereochem. at both chiral centers. The method involves novel precursor compds.

L67 ANSWER 2 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 215672-63-2 REGISTRY
CN Butanamide, 3-hydroxy-2-methyl-, (2R,3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
DR 238434-34-9
MF C5 H11 N O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:169389 Precursors for the production of chiral vicinal amino alcohols. Rozzell, J. David, Jr. (Biocatalytics, Inc., USA). U.S. US 5942644 A 19990824, 26 pp., Cont.-in-part of U. S. 5,834,261. (English). CODEN: USXXAM. APPLICATION: US 1997-929474 19970915. PRIORITY: US 1997-863900 19970527.

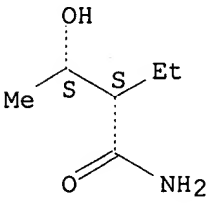
AB The disclosure describes new compns. of matter useful for the prepn. of optically active vicinal amino alcs. The compns. are chiral .beta.-hydroxy carboxamides, .beta.-hydroxy hydrazides, and .beta.-hydroxy hydroxamic acids.

REFERENCE 2: 130:3114 Method for the production of chiral vicinal aminoalcohols. Rozzell, J. David, Jr. (Biocatalytics Inc., USA). U.S. US 5834261 A 19981110, 9 pp. (English). CODEN: USXXAM. APPLICATION: US 1997-863900 19970527.

AB The disclosure describes a method for the prepn. of chiral vicinal aminoalcs. in high optical purity. The method combines the stereoselective redn. of the keto group of a .beta.-ketoacid, .beta.-keotester, or deriv. with the stereospecific rearrangement of the corresponding amide, hydroxamic acid, or hydrazide to produce chiral vicinal aminoalcs. with control of stereochem. at both chiral centers.

L67 ANSWER 3 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 215672-60-9 REGISTRY
CN Butanamide, 2-ethyl-3-hydroxy-, (2S,3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C6 H13 N O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.



3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:169389 Precursors for the production of chiral vicinal amino alcohols. Rozzell, J. David, Jr. (Biocatalytics, Inc., USA). U.S. US 5942644 A 19990824, 26 pp., Cont.-in-part of U. S. 5,834,261. (English). CODEN: USXXAM. APPLICATION: US 1997-929474 19970915. PRIORITY: US 1997-863900 19970527.

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SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US10792 19980527. PRIORITY: US 1997-863900 19970527; US 1997-929474 19970915.

AB The disclosure describes a method for the prepn. of chiral vicinal aminoalcs. in high optical purity. The method combines the stereoselective redn. of the keto group of a .beta.-keto acid, .beta.-keto ester, or deriv. with the stereospecific rearrangement of the corresponding amide, hydroxamic acid, or hydrazide to produce chiral vicinal amino alcs. with control of stereochem. at both chiral centers. The method involves novel precursor compds.

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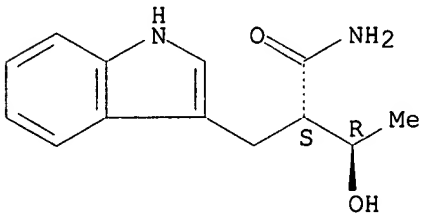
AB The disclosure describes a method for the prepn. of chiral vicinal aminoalcs. in high optical purity. The method combines the stereoselective redn. of the keto group of a .beta.-ketoacid, .beta.-keotester, or deriv. with the stereospecific rearrangement of the corresponding amide, hydroxamic acid, or hydrazide to produce chiral vicinal aminoalcs. with control of stereochem. at both chiral centers.

L67 ANSWER 4 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173655-91-9 REGISTRY
CN 1H-Indole-3-propanamide, .alpha.-(1-hydroxyethyl)-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H16 N2 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:175400 Process for producing alpha, beta-disubstituted alcohol derivatives. Murata, Masayoshi; Tsutsumi, Hideo; Ohtake, Hiroaki; Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.

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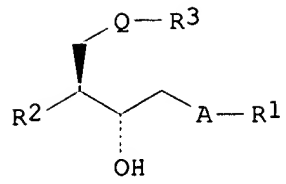

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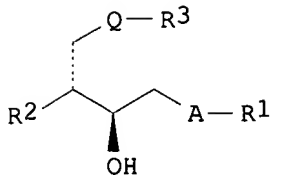

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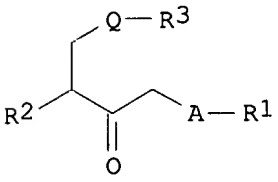

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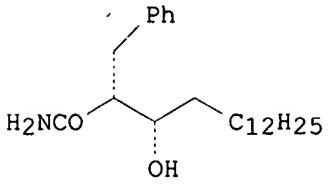

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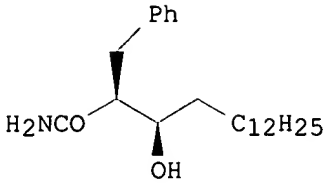


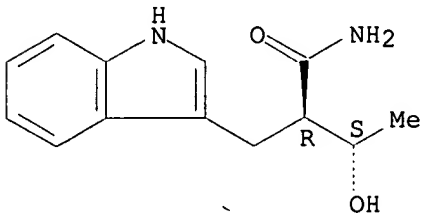
V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H, org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 - R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity for an anti-form than the conventional redn. and is industrially advantageous. Thus, a degassed soln. of 10.0 g Me 3-cyclohexylmethyl-6-methyl-3-oxoheptanoate in 50 mL MeOH was added to 28 mg p-MeC6H4SO3H and 37 mg Ru2Cl4[(S)-Binap]2NEt3 in an autoclave and the mixt. was hydrogenated at H pressure 40 atm and 40.degree. for 15 h to give, after flash chromatog., 3.66 g Me (2S,3S)-2-cyclohexylmethyl-6-methyl-3-hydroxyheptanoate of 94.4% e.e. For another example, hydrogenation of III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 5 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173655-90-8 REGISTRY

CN 1H-Indole-3-propanamide, .alpha.-(1-hydroxyethyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H16 N2 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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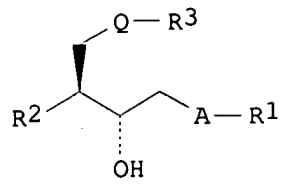
Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.
GI



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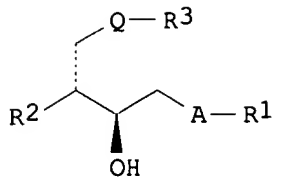

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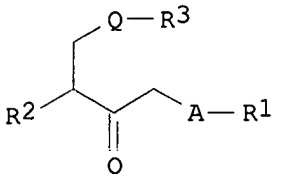

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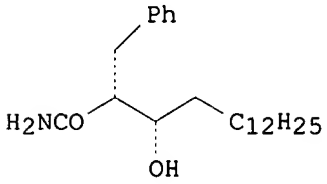

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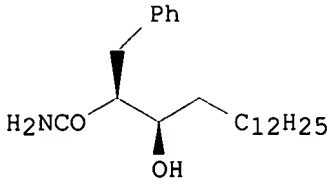


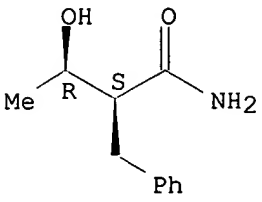
V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H, org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 - R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity for an anti-form than the conventional redn. and is industrially advantageous. Thus, a degassed soln. of 10.0 g Me 3-cyclohexylmethyl-6-methyl-3-oxoheptanoate in 50 mL MeOH was added to 28 mg p-MeC6H4SO3H and 37 mg Ru2Cl4[(S)-Binap]2NEt3 in an autoclave and the mixt. was hydrogenated at H pressure 40 atm and 40.degree. for 15 h to give, after flash chromatog., 3.66 g Me (2S,3S)-2-cyclohexylmethyl-6-methyl-3-hydroxyheptanoate of 94.4% e.e. For another example, hydrogenation of III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 6 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173655-85-1 REGISTRY
CN Benzenepropanamide, .alpha.-(1-hydroxyethyl)-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H15 N O2

SR CA
LC STN Files: CA, CAPLUS

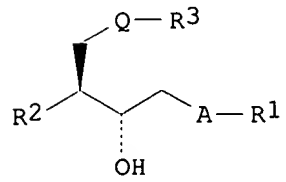
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:175400 Process for producing alpha, beta-disubstituted alcohol derivatives. Murata, Masayoshi; Tsutsumi, Hideo; Ohtake, Hiroaki;
Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.

GI



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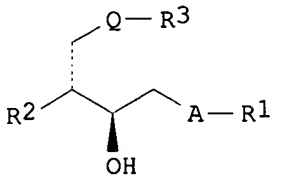

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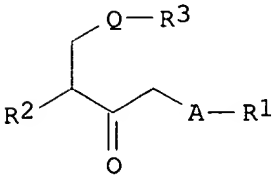

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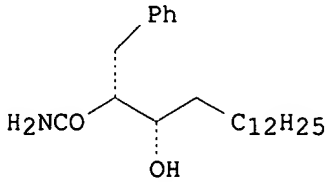
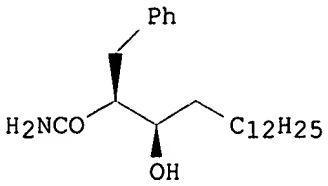


IV



V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H,

org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 -
R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity
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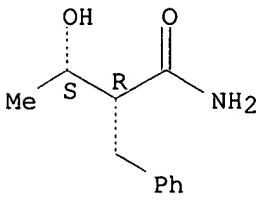
(A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25,
R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 7 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173655-84-0 REGISTRY
CN Benzenepropanamide, .alpha.-(1-hydroxyethyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H15 N O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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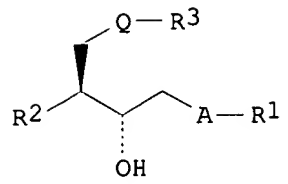
Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.
GI



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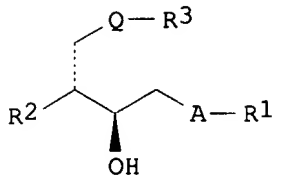

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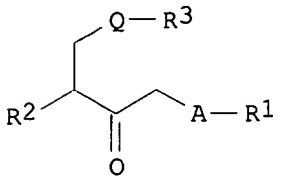

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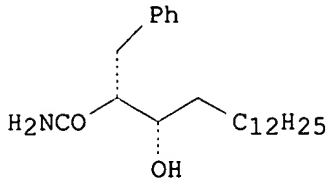

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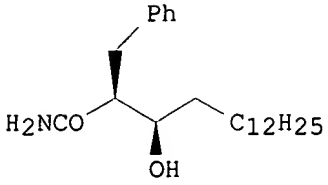


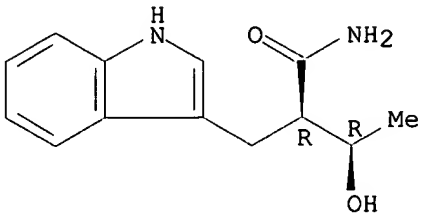
V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H, org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 -
R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity
for an anti-form than the conventional redn. and is industrially advantageous. Thus, a degassed soln. of 10.0 g Me 3-cyclohexylmethyl-6-methyl-3-oxoheptanoate in 50 mL MeOH was added to 28 mg p-MeC6H4SO3H and 37 mg Ru2Cl4[(S)-Binap]2NEt3 in an autoclave and the mixt. was hydrogenated at H pressure 40 atm and 40.degree. for 15 h to give, after flash chromatog., 3.66 g Me (2S,3S)-2-cyclohexylmethyl-6-methyl-3-hydroxyheptanoate of 94.4% e.e. For another example, hydrogenation of III
(A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25,
R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 8 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173529-73-2 REGISTRY
CN 1H-Indole-3-propanamide, .alpha.-(1-hydroxyethyl)-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H16 N2 O2
SR CA

LC STN Files: CA, CAPLUS

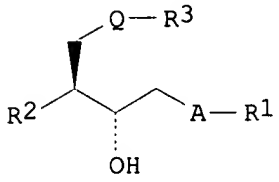
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:175400 Process for producing alpha, beta-disubstituted alcohol derivatives. Murata, Masayoshi; Tsutsumi, Hideo; Ohtake, Hiroaki;
Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.

GI



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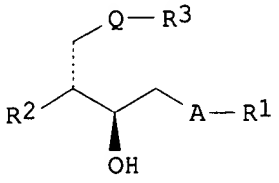

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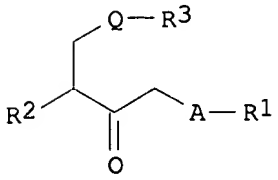

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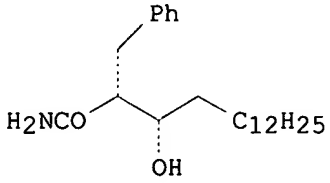

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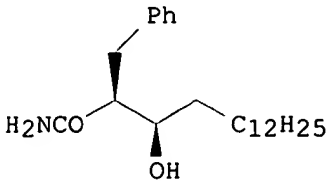
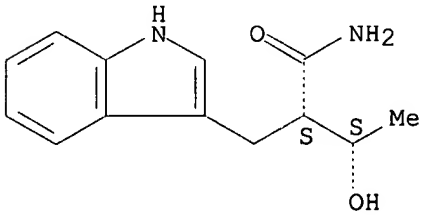


V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H, org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 - R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity for an anti-form than the conventional redn. and is industrially advantageous. Thus, a degassed soln. of 10.0 g Me 3-cyclohexylmethyl-6-methyl-3-oxoheptanoate in 50 mL MeOH was added to 28 mg p-MeC6H4SO3H and 37 mg Ru2Cl4[(S)-Binap]2NEt3 in an autoclave and the mixt. was hydrogenated at H pressure 40 atm and 40.degree. for 15 h to give, after flash chromatog., 3.66 g Me (2S,3S)-2-cyclohexylmethyl-6-methyl-3-hydroxyheptanoate of 94.4% e.e. For another example, hydrogenation of III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 9 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173529-72-1 REGISTRY
CN 1H-Indole-3-propanamide, .alpha.-(1-hydroxyethyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H16 N2 O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
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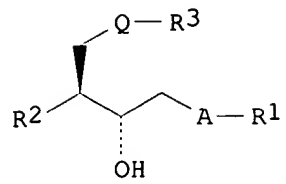
GI



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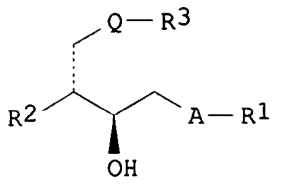

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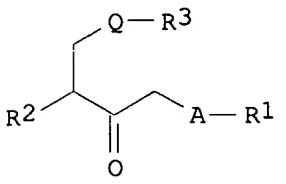

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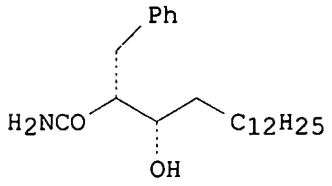

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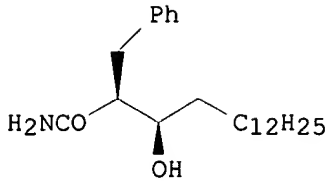


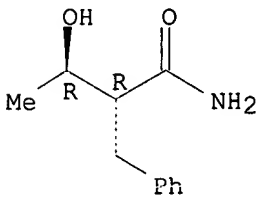
V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H, org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 - R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity for an anti-form than the conventional redn. and is industrially advantageous. Thus, a degassed soln. of 10.0 g Me 3-cyclohexylmethyl-6-methyl-3-oxoheptanoate in 50 mL MeOH was added to 28 mg p-MeC6H4SO3H and 37 mg Ru2Cl4[(S)-Binap]2NEt3 in an autoclave and the mixt. was hydrogenated at H pressure 40 atm and 40.degree. for 15 h to give, after flash chromatog., 3.66 g Me (2S,3S)-2-cyclohexylmethyl-6-methyl-3-hydroxyheptanoate of 94.4% e.e. For another example, hydrogenation of III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 10 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173529-65-2 REGISTRY

CN Benzenepropanamide, .alpha.-(1-hydroxyethyl)-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H15 N O2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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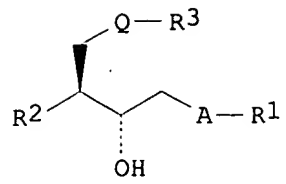
Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.
GI



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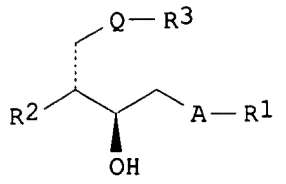

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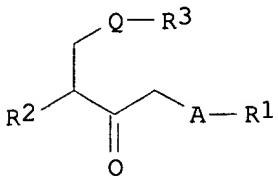

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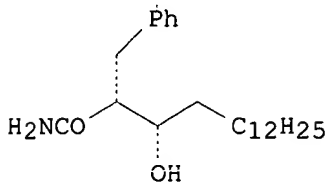

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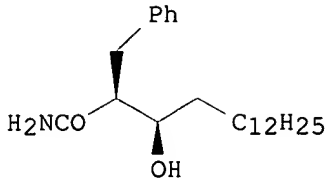


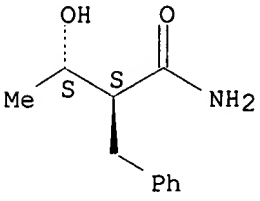
V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H, org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 - R3, A, Q = same as above) in the presence of a transition metal complex catalyst. This process gives the products with more excellent selectivity for an anti-form than the conventional redn. and is industrially advantageous. Thus, a degassed soln. of 10.0 g Me 3-cyclohexylmethyl-6-methyl-3-oxoheptanoate in 50 mL MeOH was added to 28 mg p-MeC6H4SO3H and 37 mg Ru2Cl4[(S)-Binap]2NEt3 in an autoclave and the mixt. was hydrogenated at H pressure 40 atm and 40.degree. for 15 h to give, after flash chromatog., 3.66 g Me (2S,3S)-2-cyclohexylmethyl-6-methyl-3-hydroxyheptanoate of 94.4% e.e. For another example, hydrogenation of III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) in the presence of d-camphorsulfonic acid and Ru2Cl4[(S)-Binap]2NEt3 in MeOH/EtOAc at H pressure 20 atm and 50.degree. for 2 h gave 100% a mixt. of diastereomers contg. II (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) 95.1, III (A-R1 = C12H25, R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 11 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 173529-64-1 REGISTRY
CN Benzenepropanamide, .alpha.-(1-hydroxyethyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H15 N O2

SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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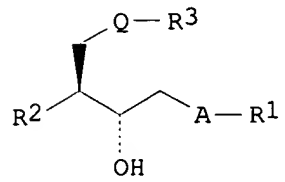
Yonishi, Satoshi (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 9527694 A1 19951019, 62 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1995-JP656 19950405. PRIORITY: JP 1994-69159 19940407; JP 1995-41753 19950301.

GI



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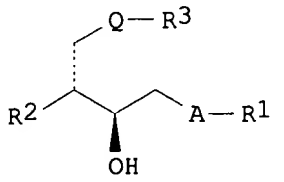

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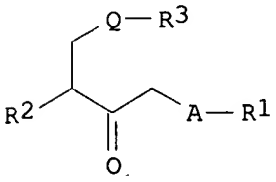

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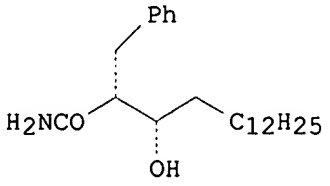

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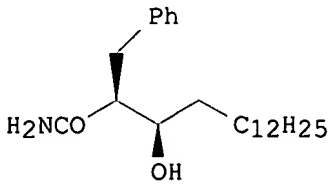

V

AB Optically active (hetero)arylhydroxyalkanamide derivs. [I and II; R1 = H,

org. group; R2 = (un)substituted carbamoyl; R3 = org. group; A, Q = lower alkylene or a single bond] are prepd. by asym. redn. of ketones (III; R1 -
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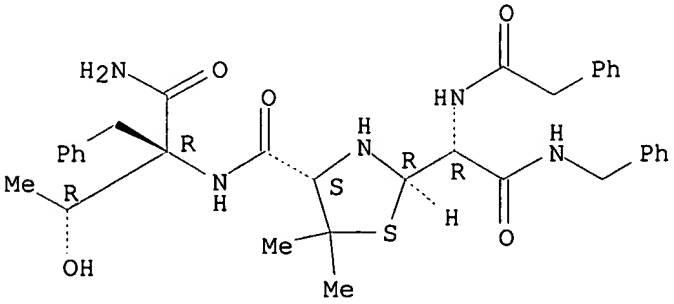
R2 = CONH2, Q-R3 = Ph) <0.1, the amide (IV) 4.9, and the amide (V) <0.1%.

L67 ANSWER 12 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 148982-37-0 REGISTRY
CN 2-Thiazolidineacetamide, 4-[[[1-(aminocarbonyl)-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-5,5-dimethyl-.alpha.-[(phenylacetyl)amino]-N-(phenylmethyl)-, [2R-[2.alpha.(R*),4.beta.(1R*,2R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H41 N5 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



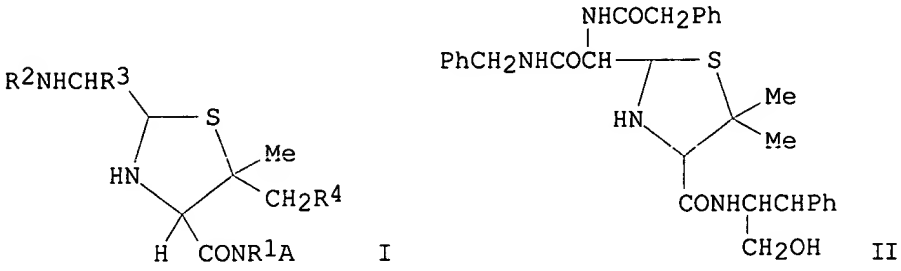
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:95513 Thiazolidine derivatives and their use as antiviral compounds. Kitchin, John; Holmes, Duncan Stuart; Humber, David Cedric; Storer, Richard; Dolan, Simon Charles; Hann, Michael Menteith; McMeekin, Peter; Petel, Binakumari; Weingarten, Gordon Gad (Glaxo Group Ltd., UK).

PCT Int. Appl. WO 9301174 A1 19930121, 90 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1992-EP1494 19920703.

PRIORITY: GB 1991-14692 19910708; GB 1991-14701 19910708.

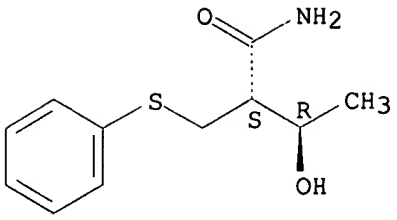
GI



AB Title compds. I (R1 = H, C1-4 alkyl, (C1-3 hydroxyalkyl)methyl; R2 = H, C1-10 alkyl, C3-8 cycloalkyl, PhCH:CHCO, Ar-C1-4 alkyl, Ar-SO3, heterocyclyl-SO2, (substituted) alkylamino, etc.; R3 = H, C1-6 alkyl, HO2C, carboxylalkyl, (substituted) aminocarbonyl, etc.; R4 = H, HO, AcO; A = hydroxyalkyl, R23COCHZNMeX wherein R23 - C1-6 alkoxy, (substituted) amino, X = CH2CH(OH)CH2CH2, etc., Z = C5-6 cycloalkylmethyl, etc.) or a salt thereof useful as virucides (no data), were prepd. [2R-[2.alpha.R,4.beta.]]-5,5-dimethyl-2-[2-oxo-1-[(phenylacetyl)amino]-2-[(phenylmethyl)amino]ethyl]-4-thiazolidinecarboxylic acid and 1-hydroxybenzotriazole in THF and DMF was treated with (R)-phenylalaninol in DMF followed by DCC and the mixt. stirred at 20.degree. for 5 1/2 h to give [2R,(2.alpha.R,4.beta.R]]-II.

L67 ANSWER 13 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 141080-26-4 REGISTRY
CN Butanamide, 3-hydroxy-2-[(phenylthio)methyl]-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H15 N O2 S
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

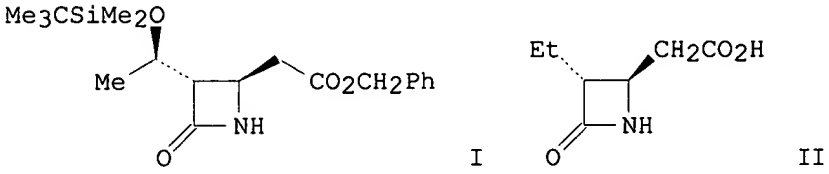
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:255360 Chemistry of O-silylated ketene acetals: a stereoselective synthesis of optically active carbapenem antibiotics, (+)-thienamycin and (+)-PS-5. Kita, Yasuyuki; Shibata, Norio; Miki, Takashi; Takemura, Yumiko; Tamura, Osamu (Fac. Pharm. Sci., Osaka Univ., Suita, 565, Japan). Chem. Pharm. Bull., 40(1), 12-20 (English) 1992. CODEN: CPBTAL. ISSN: 0009-2363.

GI

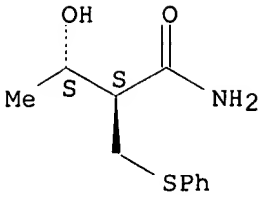


I II

AB A stereoselective synthesis of the chiral thienamycin intermediate I involving a diastereoselective Michael addn. and a silicon-induced Pummerer-type reaction is described. In a similar way, the key (+)-PS-5 intermediate II was prepd.

L67 ANSWER 14 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 137528-18-8 REGISTRY
CN Butanamide, 3-hydroxy-2-[(phenylthio)methyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H15 N O2 S
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

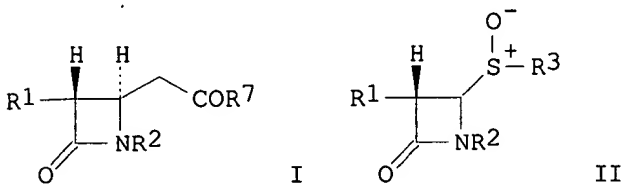
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:279696 Preparation of .beta.-lactam derivatives. Kita, Yasuyuki; Shibata, Tetsuo; Tamura, Yasumitsu (Japan). Jpn. Kokai Tokkyo Koho JP 03145460 A2 19910620 Heisei, 21 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1989-281330 19891027.

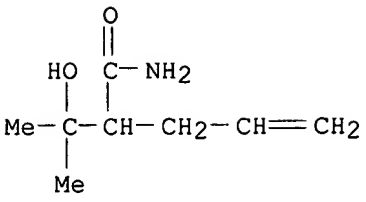
GI



I II

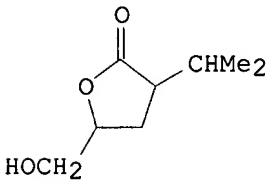
AB Acetidinoneacetates I [R1 = alkyl, (un)protected hydroxyalkyl; R2 = H, amino protecting group; R7 = phenylalkoxy, alkoxy, C(:N)CO2R8, R8 = carboxy protecting group] were prepd. by reaction of arylsulfinylazetidinones II (R3 = aryl) with H2C:CR7(OSiR4R5R6) (R4, R5, R6 = alkyl). Thus, stirring II (R1 = Me3CMe2SiOCHMe, R2 = 2,4-(MeO)2C6H3CH2, R3 = Ph) with 1-benzyloxy-1-(trimethylsilyloxy)ethylene and ZnI2 in MeCN at room temp. for 2 h gave 80.9% I [R1 = Me3CMe2SiOCHMe, R2 = 2,4-(MeO)2C6H3CH2, R7 = PhCH2O].

L67 ANSWER 15 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 92279-73-7 REGISTRY
CN 4-Pentenamide, 2-(1-hydroxy-1-methylethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H15 N O2
LC STN Files: CA, CAPLUS, TOXLIT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 101:164942 Evidence for the in vitro metabolism of allylisopropylacetamide to reactive intermediates. Mechanistic studies with oxygen-18. Prickett, Kathryn S.; Baillie, Thomas A. (Dep. Med. Chem., Univ. Washington, Seattle, WA, 98195, USA). Biomed. Mass Spectrom., 11(7), 320-31 (English) 1984. CODEN: BMSYAL. ISSN: 0306-042X.
GI



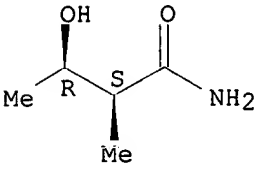
I

AB To elucidate the mechanism by which allylisopropylacetamide (AIA) [299-78-5] is converted to .gamma.-butyrolactone (I) [96-48-0] and to gain information on the nature of chem. reactive intermediates in the process, the metab. of AIA to I was investigated in 18O or H218O and the pattern of label incorporated into the product was detd. by gas chromatog./mass spectrometry. The results support the formation of AIA epoxide [92279-74-8] as an initial product of olefin oxidn. and indicate that this species undergoes rapid intramol. rearrangement to a protonated iminolactone [92279-75-9] which, in turn, is hydrolyzed to the stable I. On the other hand, the dihydrodiol metabolite of AIA [61837-27-2], which would be expected to result from direct hydrolysis of AIA epoxide, was not detected in incubation products and, furthermore, the 18O labeling data specifically exclude the possibility that it served as a precursor of I. Thus, AIA epoxide and the protonated iminolactone to which it gives rise represent reactive intermediates in the oxidn. of AIA which may play a key role in the alkylation of certain cellular constituents which accompanies metab. of AIA by liver enzymes.

L67 ANSWER 16 OF 28 REGISTRY COPYRIGHT 2001 ACS

RN 90033-13-9 REGISTRY
CN Butanamide, 3-hydroxy-2-methyl-, (R*,S*)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanamide, 3-hydroxy-2-methyl-, (R*,S*)-(.+-.)-
FS STEREOSEARCH
MF C5 H11 N O2
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Relative stereochemistry.

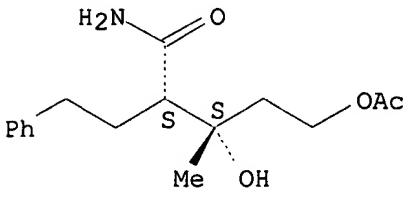


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 100:191339 Stereoselective reduction of 3-oxo amides with zinc borohydride. Ito, Yoshio; Yamaguchi, Masaru (Dep. Chem., Kyushu Univ. 33, Fukuoka, 812, Japan). Tetrahedron Lett., 24(48), 5385-6 (English) 1983. CODEN: TELEAY. ISSN: 0040-4039.
AB 2-Alkyl-3-oxo amides R1COCHR2CONR3R4 (R1 = Me, CHMe2; R2 = Me, Et; R3, R4 = H, Me, Bu, Ph, CH2Ph, cyclohexyl, CH2CH2OSiMe2CMe3) were reduced to 83-99% 2-alkyl-3-hydroxy amides HOCHR1CHR2CONR3R4 contg. 97-99% of the syn isomer, with high stereoselectivity by Zn(BH4)2.

L67 ANSWER 17 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 80344-99-6 REGISTRY
CN Benzenebutanamide, .alpha.-[3-(acetyloxy)-1-hydroxy-1-methylpropyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H23 N O4
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



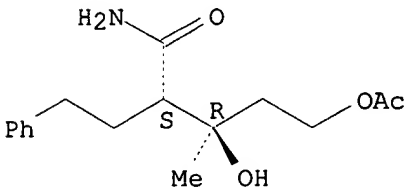
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 96:34119 Chirality of the acyl group of .beta.-hydroxy-.beta.-methylglutarylhydroxyabscisic acid. Hirai, Nobuhiro; Koshimizu, Koichi (Dep. Food Sci. Technol., Kyoto Univ., Kyoto, 606, Japan). Phytochemistry, 20(8), 1867-9 (English) 1981. CODEN: PYTCAS. ISSN: 0031-9422.

AB The .beta.-C of the acyl group of the title compd., which occurs in Robinia pseudacacia, was shown to have the R-configuration by high pressure liq. chromatog. anal. of its redn. product, mevalonolactone.

L67 ANSWER 18 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 80344-98-5 REGISTRY
CN Benzenebutanamide, .alpha.-[3-(acetyloxy)-1-hydroxy-1-methylpropyl]-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H23 N O4
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

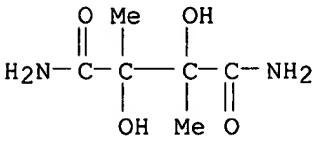


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 96:34119 Chirality of the acyl group of .beta.-hydroxy-.beta.-methylglutarylhydroxyabscisic acid. Hirai, Nobuhiro; Koshimizu, Koichi (Dep. Food Sci. Technol., Kyoto Univ., Kyoto, 606, Japan). Phytochemistry, 20(8), 1867-9 (English) 1981. CODEN: PYTCAS. ISSN: 0031-9422.

AB The .beta.-C of the acyl group of the title compd., which occurs in Robinia pseudacacia, was shown to have the R-configuration by high pressure liq. chromatog. anal. of its redn. product, mevalonolactone.

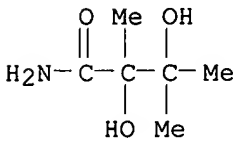
L67 ANSWER 19 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 79541-86-9 REGISTRY
CN Butanediamide, 2,3-dihydroxy-2,3-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C6 H12 N2 O4
LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 95:168109 Photoaddition of pyruvamide to 2,3-dimethyl-2-butene.
Shima, Kensuke; Hosoyama, Osamu; Tanabe, Kimiko (Fac. Eng., Miyazaki Univ., Miyazaki, 880, Japan). Nippon Kagaku Kaishi (8), 1326-8 (Japanese)
1981. CODEN: NKAKB8. ISSN: 0369-4577.
AB The photochem. addn. of MeCOCONH2 with Me2C:CMe2 in EtOH gave the 1:1 adducts CH2:CMeCMe2CMe(OH)CONH2, CH2:CMeCMe2OCHMeCONH2 (I) and Me2C:CMeCH2CMe(OH)CONH2, along with the pinacol (HOCMeCONH2)2. I was produced exclusively in low conversion expts. in MeOH. A Stern-Volmer slope of 103.6 L mol-1 for quenching by naphthalene showed that I was formed via the triplet state of pyruvamide. Rate consts. for the elementary processes were calcd.

L67 ANSWER 20 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 66483-61-2 REGISTRY
CN Butanamide, 2,3-dihydroxy-2,3-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



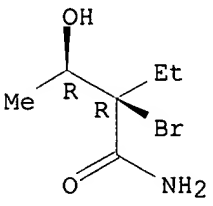
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 89:90040 Cyanohydrin synthesis of 2,3-dihydroxy-2,3-dimethylbutanoic acid. Powell, Jack E.; Osuch, Carl; Burkholder, Harvey R.; Kulprathipanja, Santi; Miller, James H.; Stadtherr, Leon G.; Baughman, Russell G. (Ames Lab., Iowa State Univ., Ames, Iowa, USA). J. Org. Chem., 43(16), 3166-9 (English) 1978. CODEN: JOCEAH. ISSN: 0022-3263.
AB From Me2C(OH)COMe (I) via cyanohydrin synthesis and subsequent hydrolysis, the intermediates Me2C(OH)CMe(OH)CN (II), Me2CClC(OH)MeC(OH):NH2+Cl- (III), Me2CClC(OH)MeCONH2 (IV), and Me2C(OH)C(OH)MeCONH2 (V) were isolated en route to Me2C(OH)C(OH)MeCO2H (VI). II reverted to I in the presence of base. In aq. NaOH or NaOMe in Et2O, III and IV gave (by HCl abstraction) 2,3-epoxy-1-hydroxy-2,3-dimethylbutanimine (VII), which was tautomeric with 2,3-epoxy-2,3-dimethylbutanamide. Acid hydrolysis of II (at 40-50.degree.) led principally to V, but at higher temps. to 3-methyl-2-butanone (VIII) via a pinacol-pinacolone type rearrangement

involving the intermediates 2,2-dimethyl-3-oxobutanamide and 2,2-dimethyl-3-oxobutanoic acid, which decarboxylated spontaneously to VIII. In the acid hydrolysis of II to obtain V and VI directly, substantial amts. of the by-product 2-hydroxy-2,3-dimethyl-3-butenoic acid were encountered; better yields of the desired products were obtained when II was first treated with 2 mol Ac2O per mol to form its diacetate and somewhat dild. HCl was used in lieu of satd. aq. HCl. The crystal structure of VII was detd.

L67 ANSWER 21 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 61472-79-5 REGISTRY
CN Butanamide, 2-bromo-2-ethyl-3-hydroxy-, (R*,R*)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanamide, 2-bromo-2-ethyl-3-hydroxy-, (R*,R*)-(.+-.)-
FS STEREOSEARCH
DR 67023-58-9
MF C6 H12 Br N O2
LC STN Files: CA, CAPLUS, TOXLIT

Relative stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

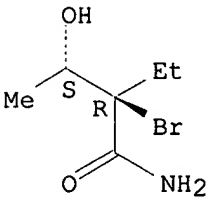
REFERENCE 1: 90:114863 Pharmacokinetic studies on monkeys after oral and intravenous dose of bromoureides and bromine-containing metabolites. Bruhns, R.; Kaeferstein, H.; Sticht, G.; Dotzauer, G. (Inst. Rechtsmed., Univ. Koeln, Cologne, Ger.). Beitr. Gerichtl. Med., 36, 497-501 (German) 1978. CODEN: BEGMA5. ISSN: 0067-5016.
AB Bromisoval [496-67-3] was hydroxylated after oral administration to rhesus monkeys. Bromoisovaleramide [7472-46-0] was not a metabolite of bromisoval; synthetic bromoisovaleramide was metabolized more slowly than bromisoval. Studies with carbromal [77-65-6] and metabolites administered i.v. showed that carbromal and hydroxycarbromal [54447-43-7] were eliminated from the blood more rapidly than hydroxycarbromide [52234-57-8] and carbromide [511-70-6]. The rate of debromination of the compds. is detd. mainly by the presence or absence of a urea group in the mol.

REFERENCE 2: 86:65286 Structure of bromine-containing metabolites of carbromal. Sticht, G.; Kaeferstein, H. (Inst. Gerichtl. Med., Univ. Koeln, Cologne, Ger.). Arch. Toxicol., 35(4), 263-73 (German) 1976.

CODEN: ATXKA8.
AB Isolation of 3 Br-contg. metabolites of carbromal [77-65-6] from human urine is described and their chem. structure is proved by comparison of their physical properties with those of synthetically prepd. substances. 2-Bromo-2-ethyl-butyramide [511-70-6], a pharmacologically active product, was the most important Br-contg. metabolite by vol. The 3-position hydroxylated metabolites, 3-hydroxycarbromal [61472-77-3] and 2-bromo-2-ethyl-3-hydroxybutyramide [61472-78-4] have same phys. properties as the synthesized DL-threo-diastereomers.

L67 ANSWER 22 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 61472-78-4 REGISTRY
CN Butanamide, 2-bromo-2-ethyl-3-hydroxy-, (R*,S*)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanamide, 2-bromo-2-ethyl-3-hydroxy-, (R*,S*)-(.+-.)-
FS STEREOSEARCH
MF C6 H12 Br N O2
LC STN Files: CA, CAPLUS, TOXLIT

Relative stereochemistry.

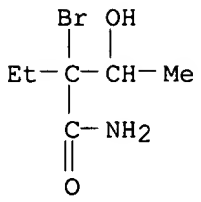


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 86:65286 Structure of bromine-containing metabolites of carbromal. Sticht, G.; Kaeferstein, H. (Inst. Gerichtl. Med., Univ. Koeln, Cologne, Ger.). Arch. Toxicol., 35(4), 263-73 (German) 1976. CODEN: ATXKA8.
AB Isolation of 3 Br-contg. metabolites of carbromal [77-65-6] from human urine is described and their chem. structure is proved by comparison of their physical properties with those of synthetically prepd. substances. 2-Bromo-2-ethyl-butyramide [511-70-6], a pharmacologically active product, was the most important Br-contg. metabolite by vol. The 3-position hydroxylated metabolites, 3-hydroxycarbromal [61472-77-3] and 2-bromo-2-ethyl-3-hydroxybutyramide [61472-78-4] have same phys. properties as the synthesized DL-threo-diastereomers.

L67 ANSWER 23 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 52234-57-8 REGISTRY
CN Butanamide, 2-bromo-2-ethyl-3-hydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Bromo-2-ethyl-3-hydroxybutyramide
FS 3D CONCORD
MF C6 H12 Br N O2

LC STN Files: CA, CAPLUS, TOXLIT



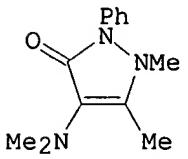
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 90:114863 Pharmacokinetic studies on monkeys after oral and intravenous dose of bromoureides and bromine-containing metabolites. Bruhns, R.; Kaeferstein, H.; Sticht, G.; Dotzauer, G. (Inst. Rechtsmed., Univ. Koeln, Cologne, Ger.). Beitr. Gerichtl. Med., 36, 497-501 (German) 1978. CODEN: BEGMA5. ISSN: 0067-5016.

AB Bromisoval [496-67-3] was hydroxylated after oral administration to rhesus monkeys. Bromoisovaleramide [7472-46-0] was not a metabolite of bromisoval; synthetic bromoisovaleramide was metabolized more slowly than bromisoval. Studies with carbromal [77-65-6] and metabolites administered i.v. showed that carbromal and hydroxycarbromal [54447-43-7] were eliminated from the blood more rapidly than hydroxycarbromide [52234-57-8] and carbromide [511-70-6]. The rate of debromination of the compds. is detd. mainly by the presence or absence of a urea group in the mol.

REFERENCE 2: 87:48577 Clinical-toxicological studies with the aid of combined gas chromatography-mass spectrometry (GC-MS). Hufnagl, D.; Ehrenthal, W. (Inst. Pharmakol. Toxikol., Univ. Saarlandes, Homburg, Ger.). Verh. Dtsch. Ges. Inn. Med., 82(2), 1977-9 (German) 1976. CODEN: VDGIA2.

GI



I

AB The use of combined gas chromatog.-mass spectrometry in clin. toxicol. anal. was illustrated by the detection of aminophenazone (I) [58-15-1], phenobarbital [50-06-6], carbromal [77-65-6], and the carbromal metabolites 2-bromo-2-ethylbutyramide [511-70-6], 2-bromo-2-ethyl-3-hydroxybutyramide [52234-57-8], and 2-ethylbutyrylurea [2274-01-3] in the blood of a patient with an overdose of Nervolitan tablets. The changes in

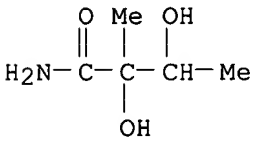
blood levels of these compds., detd. by this method, corresponded to the clin. course of the intoxication.

REFERENCE 3: 81:58082 Sensitive thin-layer chromatographic determination of bromocarbamides in body fluids. Kaeferstein, H.; Detmer, J.; Sticht, G. (Inst. Gerichtl. Med., Univ. Koeln, Cologne, Ger.). Z. Klin. Chem. Klin. Biochem., 12(4), 178-9 (German) 1974. CODEN: ZKCKAD.

AB The CHCl3 ext. of blood or urine was used for the thin-layer chromatog. detn. of hypnotic bromocarbamides, esp. carbromal (I, Et2CBrCONHCONH2) [77-65-6], and their metabolites. The limit of detection was 0.6 mg I.

A 75:15 petroleum ether-pyridine mixt. was used as developing agent. The amt. of the I metabolite bromodiethylacetamide (II, Et2CBrCONH2) [511-70-6] was a measure for the rate of intoxication. In the initial state only II traces were found, but its proportion increased up to 100%.

L67 ANSWER 24 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 40634-98-8 REGISTRY
CN Butanamide, 2,3-dihydroxy-2-methyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C5 H11 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



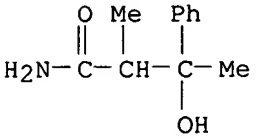
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 78:83769 Application of ion-exclusion and ion-exchange techniques in preparing 2,3-dihydroxy-2-methylbutanamide and 2,3-dihydroxy-2-methylbutanoic acid from acetoin via the cyanohydrin synthesis. Powell, J. E.; Kulprathipanja, S.; Johnson, D. A.; Burkholder, H. R. (Dep. Chem., Iowa State Univ., Ames, Iowa, USA). J. Chromatogr., 74(2), 265-8 (English) 1972. CODEN: JOCRAM.

AB Ion exclusion and ion exchange have been used to obtain substantial yields of 2,3-dihydroxy-2-methylbutanamide and 2,3-dihydroxy-2-methylbutanoic acid, resp., following acid hydrolysis of acetoin cyanohydrin. Acetoin with anhyd. HCN appeared to be stereospecific, since the process yielded an unexpectedly high percentage of (2S,3R)-2,3-dihydroxy-2-methylbutanoic and (2R,3S)-2,3-dihydroxy-2-methylbutanoic acid.

L67 ANSWER 25 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 14300-99-3 REGISTRY
CN Hydrocinnamamide, .beta.-hydroxy-.alpha.,.beta.-dimethyl- (6CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD

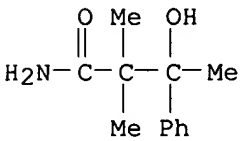
MF C11 H15 N O2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 67:21562 Modified Reformatskii reaction between amides of .alpha.-bromo-substituted carboxylic acids and aromatic aldehydes and ketones. Sivertseva, A. V. (Khim.-Farm Inst., Leningrad, USSR). Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol., 9(6), 915-17 (Russian) 1966. CODEN: IVUKAR.
GI For diagram(s), see printed CA Issue.
AB cf. CA 54: 20976d. The following compds. were obtained by reaction of the
corresponding aldehyde or ketone with an .alpha.-bromo-substituted alkyl or dialkyl acetamide with Zn in dry C6H6 for 1.5-3 hrs.: 70.7% PhCH(OH)CHEtCONH2, m. 117-18.degree.; 51.6% PhCH(OH)CHMeCON:CHPh, m. 169.5-70 or 145-6.degree. (2 isomers); 64.8%
PhCH:CHCH(OH)CMe2CON:CHCH:CHP
h, m. 162-3.degree.; 42.7% p-MeOC6H4CH(OH)CHMeCON:CHC6H4OMe-p, m. 190-90.5.degree.; 61.8% PhMeC(OH)CMe2CONH2, m. 142-3.degree.; 52.6% PhMeC(OH)CHMeCONH2, m. 160-1.degree.; 50.6% I (R = R1 = Me), m. 148.5-9.0.degree.; 51.1% I (R = H, R1 = Et), m. 130-1.degree.; 61.2% II, m. 146-6.5.degree.. In the case of the treatment of PhCOMe with .alpha.-bromodiethyl-acetamide, no reaction was observed.

L67 ANSWER 26 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 14300-98-2 REGISTRY
CN Hydrocinnamamide, .beta.-hydroxy-.alpha.,.alpha.,.beta.-trimethyl- (8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C12 H17 N O2
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



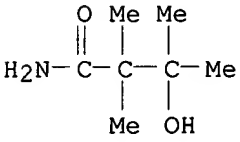
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 67:21562 Modified Reformatskii reaction between amides of .alpha.-bromo-substituted carboxylic acids and aromatic aldehydes and ketones. Sivertseva, A. V. (Khim.-Farm Inst., Leningrad, USSR). Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol., 9(6), 915-17 (Russian) 1966. CODEN: IVUKAR.

GI For diagram(s), see printed CA Issue.

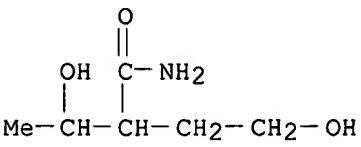
AB cf. CA 54: 20976d. The following compds. were obtained by reaction of the corresponding aldehyde or ketone with an .alpha.-bromo-substituted alkyl or dialkyl acetamide with Zn in dry C6H6 for 1.5-3 hrs.: 70.7% PhCH(OH)CHEtCONH2, m. 117-18.degree.; 51.6% PhCH(OH)CHMeCON:CHPh, m. 169.5-70 or 145-6.degree. (2 isomers); 64.8% PhCH:CHCH(OH)CMe2CON:CHCH:CHPh, m. 162-3.degree.; 42.7% p-MeOC6H4CH(OH)CHMeCON:CHC6H4OMe-p, m. 190-90.5.degree.; 61.8% PhMeC(OH)CMe2CONH2, m. 142-3.degree.; 52.6% PhMeC(OH)CHMeCONH2, m. 160-1.degree.; 50.6% I (R = R1 = Me), m. 148.5-9.0.degree.; 51.1% I (R = H, R1 = Et), m. 130-1.degree.; 61.2% II, m. 146-6.5.degree.. In the case of the treatment of PhCOMe with .alpha.-bromodiethyl-acetamide, no reaction was observed.

L67 ANSWER 27 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 4237-82-5 REGISTRY
CN Butyramide, 3-hydroxy-2,2,3-trimethyl- (7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H15 N O2
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L67 ANSWER 28 OF 28 REGISTRY COPYRIGHT 2001 ACS
RN 997-14-8 REGISTRY
CN Butyramide, 3-hydroxy-2-(2-hydroxyethyl)- (7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C6 H13 N O3
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L68           3 L67

=> d 1-3

L68  ANSWER 1 OF 3  CAOLD  COPYRIGHT 2001 ACS
AN   CA63:14696h  CAOLD
TI   ethylenic nitriles - (III) dimethylation of ethylenic nitriles (1), (IV)
     mechanism of fragmentation or of lactonization of nitriles, amides, and
     .alpha., .alpha.-dimethylated .beta.,.gamma.-ethylenic acids in acid
     medium
AU   Fleury, Jean P.; Bader, A.
IT    109-75-1    594-88-7   1119-15-9   4168-01-8   4168-02-9   4168-03-0
     4168-04-1   4173-75-5   4177-00-8   4177-01-9   4177-03-1   4177-05-3
     4177-06-4   4237-81-4   4237-82-5   4237-83-6   4258-18-8
     4258-20-2   4467-04-3   4786-14-5   4786-15-6   4786-16-7   4786-18-9
     4786-19-0   4786-20-3   4786-23-6   4786-24-7   4786-25-8   4786-26-9
     4786-27-0   4786-28-1   4786-29-2   4786-34-9   4786-35-0   4786-36-1
     4786-37-2   4786-38-3   4786-39-4   4786-40-7  90204-38-9

L68  ANSWER 2 OF 3  CAOLD  COPYRIGHT 2001 ACS
AN   CA62:1622h  CAOLD
TI   synthesis and rearrangement of 3-vinyl-2-pyrrolidone
AU   Cummings, William A. W.; Davis, A. C.
```

IT 921-84-6 930-92-7 930-95-0 931-44-2 932-26-3 932-45-6
932-46-7 932-47-8 932-48-9 934-43-0 934-44-1 936-01-6
936-06-1 936-07-2 936-12-9 936-13-0 936-82-3 936-83-4
936-84-5 939-75-3 941-16-2 942-11-0 943-10-2
997-14-8 1003-88-9 1006-38-8 1009-29-6 1016-65-5
1023-30-9 1196-84-5 1447-91-2 3920-62-5 3920-63-6 6773-85-9
6820-01-5 31423-99-1 31424-37-0 90204-90-3

L68 ANSWER 3 OF 3 CAOLD COPYRIGHT 2001 ACS
AN CA54:10941b CAOLD
TI synthesis of amebicidal agents
AU Warman, Kamla; Kachru, C. N.
IT **14300-99-3** 18149-09-2 20628-07-3 24506-17-0 55007-22-2
58404-64-1 90921-37-2 91246-99-0 99075-48-6 103095-28-9 103203-48-1
103853-34-5 104179-19-3 104338-20-7 104338-22-9 105972-10-9

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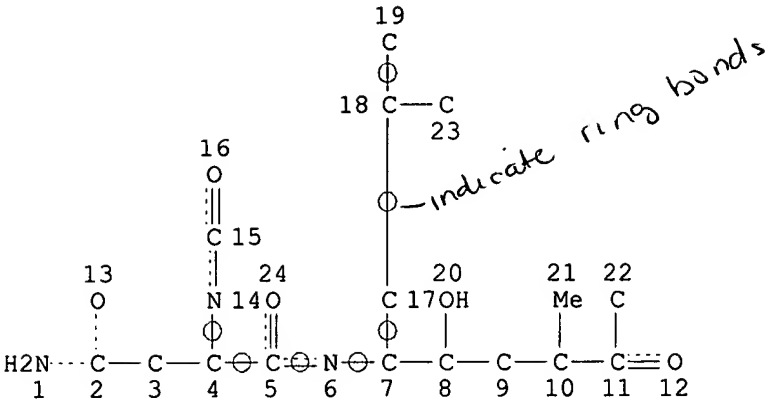

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